REMARKS

I. Support for Amendments

Claims 1-39 have been cancelled and claims 40-58 have been added to more accurately define the invention. Support for new claims 40-58 is found throughout the specification, for example, on page 6, line 16 to page 7, line 2, page 10, lines 5-11, page 15, lines 17-23, page 16, lines 3-13, pages 57-59, page 61, lines 5-18, and Figure 11. Accordingly, no new matter is added by this Amendment and entry thereof is respectfully requested.

II. Summary of Two Restriction Requirements

Restriction Requirement I

The first Restriction Requirement was mailed on July 1, 2004. In this, the Examiner had requested that the Applicants elect Group I, in which the claims are directed to a method of identifying an agent that modulates GD domain mediated **heterodimerization** OR Group II in which the claims are directed to a method of identifying an agent that modulates GD domain mediated **homodimerization**. Applicants elected Group I, the **heterodimerization** group.

The Examiner pointed out that the "GD domain protein can be any SEQ ID NO: 35-41." See Page 3, lines 14-15 of the Restriction Requirement. The Examiner further stated that one SEQ ID from SEQ ID NOS: 35-41 should be elected as a protein

containing the GD domain. In other words, all of the polypeptides characterized by SEQ ID NOS: 35-41 correspond to GD proteins.

The Examiner pointed out that the combination of "GD protein type" is "Bak, Bcl-xl, [B]ax, or Bipla." See page 3, lines 5-6 of the Restriction Requirement. In other words, GD proteins can heterodimerize with Bcl-x_L or Bax.

As stated above, in response to the Restriction Requirement, the Applicants elected Group I, and further elected SEQ ID NO: 36. The GD domain proteins can heterodimerize with Bcl-x_L or Bax, but not with any of SEQ ID NOS: 35, or 37-41.

Restriction Requirement II

In the second Restriction Requirement dated October 18, 2004, the Examiner has stated that "[b]y definition heterodimerization must be between two different sequences." The Examiner has suggested that the Applicants are directed to elect a single combination of sequences chosen from SEQ ID NOS: 35-41. However, as described above, these sequences, if elected, would not heterodimerize with SEQ ID NO: 36.

Hence, if Applicants elect any one of the sequences from SEQ ID NOS: 35-41, Applicants would be electing a homodimerizing partner instead of a heterodimerizing partner, contrary to the desire of the examiner in the second Restriction Requirement.

To prevent any further inconsistency and to make the claims consistent with the elected Group I invention and SEQ ID NO: 36, Applicants have amended the claims and a detailed Response to the Restriction Requirement is provided below.

III. Explanation of Sequence Listings in SEQ ID NOS: 35-41

For the convenience of the Examiner, Applicants hereby provide an explanation of the sequences of SEQ ID NOS: 35-41. SEQ ID NOS: 35, 36, 37, and 38 are all peptides, which correspond to the **Bak GD** domain (variants beginning/ending at different points). SEQ ID NO: 39 correlate to 20 amino acids, which correspond to the **GD** domain of **Bcl-w** (an anti-apoptotic Bcl-2/Bcl-xL family member). SEQ ID NO: 40 correlates to 20 amino acids, which correspond to the **GD** domain of **Bax** (a pro-apoptotic Bcl-2 family member). SEQ ID NO: 41 correlate to 20 amino acids, which corresponds to the **GD** domain of **Bip1a** (a pro-apoptotic Bcl-2 family member).

IV. Response to Restriction Requirement

In response to the Restriction Requirement mailed October 18, 2004, Applicants elect Group I. Moreover, Applicants further elect SEQ ID NO: 36 and Bcl-x_L as the combination of sequences to be examined in Group I.

The Examiner's restriction requirement required the election of Group I or Group II. The restriction requirement further required that if Group I was elected, then a single combination of nucleotide sequences also had to be elected. In particular, the Examiner stated that "[i]n each case, the sequence election will be considered to be an election of the corresponding single named GD Domain protein type (or combination thereof (E.g. Back, Bcl-xl, [B]ax or Bip1a))." Applicants' election of Group I and the single combination of SEQ ID NO:36 and Bcl-x_L is reflected in newly added claims 40-58. This claim is fully responsive to the restriction requirement and is consistent with Applicants' election.

In particular, Applicants note that upon further review of the claims, the specification describes the heterodimerization between SEQ ID NO: 36 and Bax or Bcl-x_L. *See* page 16, lines 3-13, pages 57-59, and page 61, lines 5-18. Applicants respectfully point out that the claims inadvertently suggested that there was heterodimerization between SEQ ID NO: 36 with any of SEQ ID NOS: 35 or 37-41. However, upon further examination of the specification and consultation with the researchers, it is clear that SEQ ID NO: 36 is capable of heterodimerizing with Bax or Bcl-x_L. For example, SEQ ID NO: 36 is a Bak polypeptide comprising the GD domain. *See* page 15, lines 17-23. The specification provides that the Bak GD domain is involved in the heterodimerization of Bak with other proteins, such as Bcl-x_L. For example, at page 10, lines 5-11, the specification states that:

> In another aspect, the present invention is related to the surprising discovery that the Back GD domain is involved in and sufficient for homodimerization and heterodimerization of Back. **Nonlimiting examples of Back GD domain dimerization include** Back (homodimerization), Bax (heterodimerization with a different killer protein) and **Bcl-x_L (heterodimerization with a survival protein).**

In addition, the examples further support the heterodimerization between SEQ ID NO:36 and Bcl-x_L. Specifically, in Section C on page 58, line 16 to page 59, line 2, the specification provides the following:

> To illustrate presently preferred embodiments of the invention for the identification of useful compounds, compositions and agents employing GD domain variants as described herein, a high through-put screening assay as described herein was carried out using exemplary and presently preferred variants of the GD domain peptide PSSTMGQVGRQLAIIGDDINRRYDSEFQ (amino acid residues 67-94; [SEQ ID NO: 2]) derived from Back, and lacking the first four and last five amino acids (amino acid residues 71-89; MGQVGRQLAIIGDDINRRY [SEQ ID NO: 35]), or lacking the first three and last five amino acids (amino acid residues 70-89; TMGQVGRQLAIIGDDINRRY; [SEQ ID NO: 36]).

In the discussion of the in vitro binding assay in Section C on page 61, lines 5-18, the specification provides that SEQ ID NO: 36 is used to heterodimerize with Bcl-x_L in the screening assay as follows:

> An in vitro binding assay as described herein can be used to screen for compounds, compositions and agents that disrupt GD domain-mediated interactions.
>
> GST-Bcl-x_L or GST-BC1-2 is incubated with a labeled GD domain-containing protein in the presence of a test compound. Resulting protein complexes are captured on GSH-agarose beads and the amount of labeled interacting protein is measured. Compounds that block binding will inhibit complex formation.
>
> In a specific example, the inhibition of the interaction of GST-Bcl-x_L and ^{35}S-methionine-labeled Back by a 20-amino acid Back GD domain peptide (amino acid residues 70-89; TMGQVGRQLAIIGDDINRRY; [SEQ ID NO: 36]) is shown in FIG. 11.

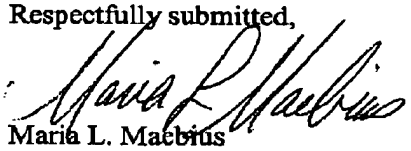
Newly added claims 40-58 correct the inadvertent error and now clarify that SEQ ID NO: 36 heterodimerizes with, *inter alia*, Bcl-x_L in the methods of the present invention involving heterodimerization assays. New claims 40-58 are consistent with an election of Group I where the single combination of sequences is SEQ ID NO: 36 and Bcl-x_L. Applicants respectfully request the entry and examination of new claims 40-58.

Furthermore, in view of Applicants' election of Bcl-x_L as the heterodimerizing partner for SEQ ID NO: 36 in this application, the newly added claims only refer to Bcl-x_L. However, Applicants reserve the right to pursue claims where the heterodimerizing partner is SEQ ID NO: 36 and Bax as well as to pursue the other non-elected subject matter in another application.

V. Conclusion

Although no fee is believed to be due at this time, the Commissioner is authorized to deduct any fee that may be necessary to maintain the pendency of this application from PTO Deposit Account No. 08-0219. Should there be any questions, the undersigned can be contacted at the below-listed telephone number.

Respectfully submitted,



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